10578449

PREPARATION AND COMPOSITION OF INTER-ALPHA INHIBITOR PROTEINS FROM HUMAN PLASMA FOR THERAPEUTIC USE

RELATED APPLICATION

This application contains subject matter that is related to that disclosed in provisional patent application Ser. No. ~~60/~~60/518,366 ~~_____~~ filed November 8, 2003, entitled, "Preparation and Composition of Inter-alpha Inhibitor Proteins from Human Plasma for Therapeutic Use," the disclosure of which application is incorporated herein in its entirety by this reference.

GOVERNMENT SUPPORT

A portion of this invention may have been supported by National Institutes of Health grants RO1 GM053008, R01 GM057468, and R43 GM065667.

BACKGROUND OF THE INVENTION

The inter-alpha inhibitor protein (IαIp) family is a group of plasma-associated serine protease inhibitors. Members of this family are composed of heavy and light polypeptide subunits that are covalently linked by a glycosaminoglycan. The light chain, also called bikunin, is responsible for the serine protease inhibitory activity of the molecules. The name "bikunin" reflects the presence of 2 protease-inhibiting domains of the Kunitz type. In normal plasma, bikunin is found mostly in a complex form as inter-alpha inhibitor (IαI), which has a molecular weight of 225 kDa, and pre-alpha inhibitor (PαI), which has molecular weight of 120 kDa. In IαI, bikunin is linked to 2 heavy polypeptide chains, H1 and H2, whereas, in PαI, only a single heavy chain (H3) is linked to bikunin. In these complexed forms, bikunin remains inactive until its release by partial proteolytic degradation, a mechanism that serves as a means to regulate activity. After cleavage from the complex, the activated bikunin is cleared rapidly from plasma by glomerular filtration, a process that is facilitated by its low molecular weight and by receptor-mediated uptake. US Patent Nos. 6,489,128 and 6,660,482 are related to the use of diagnosing cancer and sepsis, respectively. Methods of inhibiting metastases and of treating sepsis are also